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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/846,933	04/30/97	CLELAND J	P0825BC3

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EXAMINER	
HINES,J	
ART UNIT	**PAPER NUMBER**
1645	29

DATE MAILED: 04/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/846,933	Cleland et al.
Examiner	**Group Art Unit**
Ja-Na Hines	1645

☒ Responsive to communication(s) filed on *Feb 5, 2001*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1, 4-9, and 23-28* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 4-9, and 23-28* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

2. In view of the response filed on December 12, 1999, PROSECUTION IS HEREBY REOPENED. New Grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(a) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(b) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Amendment Entry

3. The amendment filed February 5, 2001 has been entered. Claims 1, 4, 6-7 and 23-27 have been amended. Claims 1, 4-9, 23-28 are pending.

Withdrawal of Rejections

4. Claims 1, 4-9, 23-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn in view of applicants amendments.

5. Claims 1, 4, 9 and 23-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Floy et al., is withdrawn in view of applicants amendments and arguments.

6. Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Floy et al., Sanders et al., (as applied to claims 1, 4, 9 and 23-28) in view of Immunization Practices Advisory Committee is withdrawn in view of applicants and amendments.

7. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Floy et al., Sanders et al., (as applied to claims 1, 4, 9 and 23-28) in view of Immunization Practices Advisory Committee and in further view of Newman et al., is withdrawn in view of applicants and amendments.

Response to Arguments

8. Applicant's arguments filed February 5, 2001 have been fully considered but they are not persuasive.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1, 4-9 and 23-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sanders et al., in view of Elkridge et al., and further in view of Jeffery et al., is maintained. In applicants response, "Applicants wish to emphasize that claim 1 is an open-ended "comprising" claim and therefore reads on any composition including at least one such population of microspheres, regardless of the presence of other microsphere populations or other components" Then applicants argue that Elkridge et al., manipulates the phasic burst by mixing different populations of microspheres, however applicant states that mixed populations are within the scope of claim 1. Therefore, Elkridge et al., teaches homogenous populations.

Applicants state that Elkridge et al., used mixed populations of microspheres wherein the mixture of 1-10um in diameter and 20-125um in diameter, however Elkridge et al., also used homogenous populations wherein the homogenous population was 1-10um and another homogenous population of 20-125um diameter microspheres (page 290 and fig. 2). Therefore, Elkridge et al., clearly teaches the use of homogenous populations.

Next, applicants argue that triphasic release is not taught by the combination of references. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. In this case, Sanders et al., teaches that the microspheres have a triphasic release over 90 days wherein there is an initial burst, followed by a slow release period where less than 0.4 ug/day of the antigen is released, followed by a final release from about day 38 to day 90 (see figure 4a). Sanders et al., teaches a biological profile wherein the is a 50:50 copolymer ratio and an inherent viscosity which was 0.38 dL/g for the microspheres (see figure 1). Sanders et al., showed the effect of size of the 55:45 copolymer microspheres wherein the microspheres used were either large, 80-150ug or small, 30-50ug, see figure 7. When the composition is adjusted to 50:50 mol% d,l-lactide-co-glycolide (Fig. 4b), there is partial overlap between the primary and tertiary phases, however even in the system providing continuous efficacy in the rat, the data clearly indicates a triphasic compound release as shown by release profile (fig. 2), and by nonlinearity in the plasma profiles (fig. 3a).

Applicant argues that Jeffery et al., teaches the use of small microspheres, therefore there is no reason to combine Jefferies with Sanders et al., and Elkridge et al. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re*

Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Jefferies et al., teaches the use of antigen delivery systems using poly(lactide-co-glycolide) microparticles with entrap antigens or adjuvants as controlled release vaccines (page 362). These vaccines may be designed to release entrapped antigens at predetermined intervals following a single immunizations thereby eliminating the need for booster doses. Jefferies et al., used smooth spherical microparticles 1-2um in diameter, however claim 1 does not exclude the use of small microparticles. Claim 1 says the median diameter is about 20-100um, it does not exclude the use of including these homogenous microspheres because it contains open-ended claim language.

Therefore, in light of the arguments presented above, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use various volumes of antigen incorporated into PLGA, as taught by Jeffery et al., to produce a composition with different concentrations of antigen that can be released over a variety of time periods in a homogenous population with the ratios stated by the claims as taught by Sanders et al., in view of Elkridge et al.

10. Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sanders et al., in view of Elkridge et al., and further in view of Jeffery et al., (as applied to claims 1, 4, 9 and 23-28) and further in view of Wang et al., is maintained.

Applicants argue that Wang et al., does not teach or suggest triphasic release profile meeting the claim limitations of the specification .However, as discussed above, Sanders et al., in view of Elkridge et al., and further in view of Jeffery et al., teach the use of homogenous populations of microspheres encapsulating an antigen having the recited release profiles. Wang et al., teaches that it is known in the art of vaccination to combine adjuvants with antigens and to combine the two elements for release from microsphere. Therefore it would have been obvious at the time of applicants invention to encapsulate an adjuvant in the antigen-encapsulated microspheres taught in the prior art because the adjuvant would be expected to enhance the immune response of a vaccine composition and may add the advantage of a higher initial release of the antigen and more efficient protein loading as taught by Wang et al.

11. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sanders et al., in view of Elkridge et al., and further in view of Jeffery et al., (as applied to claims 1, 4, 9 and 23-28) and further in view of Newman et al., is maintained. In response to applicant's argument that there is no suggestion to combine the references because Newman does not teach or suggest a homogeneous population of microspheres encapsulating an antigen having the recited release profiles. However, Sanders et al., in view of Elkridge et al., and further in view of Jeffery et al., teach the use of homogenous populations of microspheres encapsulating an antigen having the recited release profiles. The cited references however do not teach the adjuvant QS21. Newman et al., teaches that QS21 has the advantage of augmenting both antibody responses and cell-

mediated immunity and established immunological memory. In this case, no more then routine skill was required to use the known adjuvant QS21, as taught by Newman et al., in vaccine composition with a homogenous populations of microspheres encapsulating an antigen having the recited release profiles as taught by Sanders et al., in view of Elkridge et al., and further in view of Jeffery et al., since Newman et al., teaches QS21 can be used as a safe non-toxic adjuvant which augments both antibody responses and cell-mediated immunity.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines

April 19, 2001

4/19/01

JENNIFER E. GRASER
PRIMARY EXAMINER